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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/560,533	12/13/2005	Anna Fernandez Serrat	3378-0101	6463

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ROTHWELL, FIGG, ERNST & MANBECK, P.C.  
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SUITE 800  
WASHINGTON, DC 20005

EXAMINER
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MURRAY, JEFFREY H

ART UNIT	PAPER NUMBER
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1624

NOTIFICATION DATE	DELIVERY MODE
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06/02/2010

ELECTRONIC

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PTO-PAT-Email@rfem.com

<b>Office Action Summary</b>	<b>Application No.</b> 10/560,533	<b>Applicant(s)</b> FERNANDEZ SERRAT ET AL.	
	<b>Examiner</b> JEFFREY H. MURRAY	<b>Art Unit</b> 1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 04 May 2010.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 12-14 and 46 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 12, 14 and 46 is/are rejected.
- 7) ☒ Claim(s) 13 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All    b) ☐ Some \*    c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |   |   |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)         | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)         | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____   | 6) <input type="checkbox"/> Other: _____                          |

## **DETAILED ACTION**

### ***Status of Claims***

Claims 12-14 and 46 are pending in this application. Claims 1-11 and 15-45 have been cancelled. This action is in response to the applicants' response to a final office action filed on January 6, 2010.

### ***Withdrawn Rejections/Objections***

Applicant is notified that any outstanding rejection/objection that is not expressly maintained in this office action has been withdrawn or rendered moot in view of applicant's amendments and/or remarks.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

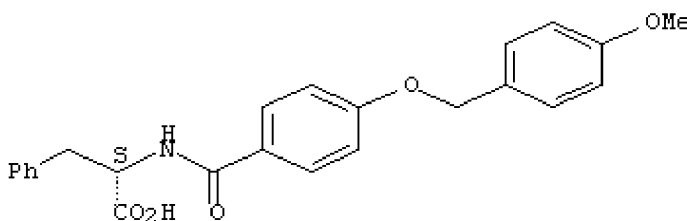
Claims 12, 14, and 46 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kundu, et. al., Combinatorial Chemistry and High Throughput

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Screening (2002), 5(7), 545-550, in view of *In re Hass et al.* (CCPA 1944) 141 F2d 122 and 127, 60 USPQ 544 and 548; and *In re Henze* (CCPA 1950) 181 F2d 198, 85 USPQ 261.

The prior art teaches the following compound 38 on page 546:

RN 524048-71-3 CAPLUS  
 CN L-Phenylalanine, N-[4-[(4-methoxyphenyl)methoxy]benzoyl]- (CA INDEX NAME)  
 Absolute stereochemistry.



The CCPA has defined a homologous series as a family of chemically related compounds, the composition of which varies from member to member by a -CH<sub>2</sub> (one atom of carbon and two hydrogen). *In re Coes, Jr.* (CCPA 1949) 173 F2d 1012, 81 USPQ 369. The Court of Appeals for the District of Columbia applied a broader definition and defined a homolog (homologue) as a member of a series of compounds in which each member differs from the next member by a constant number of atoms. Carr. Pats.v. Deutsche Gold-und-Silber, etc. (CADC 1968) 397 F2d 656, 157 USPQ 549.

The "Hass-Henze Doctrine" evolved from three CCPA cases, viz., *In re Hass et al.* (CCPA 1944) 141 F2d 122 and 127, 60 USPQ 544 and 548; and *In re Henze* (CCPA 1950) 181 F2d 198, 85 USPQ 261. In the *Henze* decision, the Court said:

"The nature of homologues and the close relationship the physical and chemical properties of one member of a series bears to adjacent members is such that a presumption of unpatentability arises against a claim

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directed to a composition of matter, the adjacent homologue of which is old in the art. The burden is on the applicant to rebut that presumption by a showing that the claimed compound possesses unobvious or unexpected beneficial properties not actually possessed by the prior art homologue. It is immaterial that the prior art homologue may not be recognized or known to be useful for the same purpose or to possess the same properties as the claimed compound. The CCPA concluded that because the characteristics normally possessed by members of a homologous series are principally the same, varying gradually from member to member, chemists knowing the properties of one member of a series would in general know what to expect in adjacent members so that a mere difference in degree is not the marked superiority which will ordinarily remove the unpatentability of adjacent homologues of old substances. Contra, where no use for the prior art compound is known. *In m Sterniski* (CCPA 1971) 444 F2d 581, 170 USPQ 343, and cases cited therein. Whether a compound is patentable over a prior art homologue or isomer is a question to be decided in each case. *In re Hass et al.*, *supra*."

The 'Hass-Henze Doctrine' stands for the proposition that, "If that which appears at first blush to be obvious though new is shown by evidence not to be obvious then the evidence prevails over surmise or unsupported contention and rejection based on obviousness must fail." *In re Papesch* (CCPA 1963) 315 F2d 381, 137 USPQ 43, 48. The presumption that homologues are unpatentably obvious is an inference of fact, viz., that adjacent homologs are expected to have similar properties which places a 'burden of persuasion' on the applicant who asserted a contrary fact. *In re Mills* (CCPA 1960) 281 F2d 218, 126 USPQ 513.

Compounds that differ only by the presence of an extra methyl group are homologs. Homologs are of such close structural similarity that the disclosure of a compound renders prima facie obvious its homolog. The homolog is expected to be capable of preparation by the same method and to have the same properties. This expectation is then deemed the motivation for preparing homologs. Homologs are

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obvious even in the absence of a specific teaching to methylate, *In re Wood* 199 USPQ 137; *In re Hoke* 195 USPQ 148; *In re Lohr* 137 USPQ 548; *In re Magerlein* 202 USPQ 473; *In re Wiechert* 152 USPQ 249; *Ex parte Henkel* 130 USPQ 474; *In re Fauque* 121 USPQ 425; *In re Druey* 138 USPQ 39. In all of these cases, the close structural similarity of two compounds differing by only one (or two) methyl groups sufficed; no specific teaching to methylate was present or required. None of these cases has been overruled and indeed the examiner is unaware of any post *Lohr* case in which motivation is required to put a methyl group on an old compound.

Here the prior art compound contains an -OMe substituent on the phenyl ring. However, the claims of the current application permit this group to be a (C<sub>1</sub>-C<sub>4</sub>)-alkoxyl group. Therefore an ethoxy or propoxy substitution would be attempted by anyone skilled in the art who was attempting to make the compounds of Formula (I). The claims of the current application are obvious because the addition of a -CH<sub>2</sub>- group would have yielded predictable results in the process to one of ordinary skill in the art at the time of the invention.

Claims 12, 14, and 46 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kundu, et. al., *Combinatorial Chemistry and High Throughput Screening* (2002), 5(7), 545-550, in view of *In re Norris* (CCPA 1950) 179 F2d 970, 84 USPQ 458.

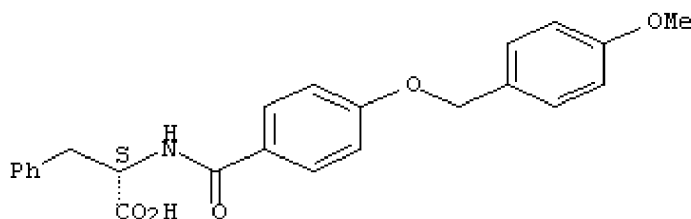
The prior art teaches the following compound 38 on page 546:

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RN 524048-71-3 CAPLUS

CN L-Phenylalanine, N-[4-[(4-methoxyphenyl)methoxy]benzoyl]- (CA INDEX NAME)

Absolute stereochemistry.



It is well known in the art that compounds having the same radical at different positions on the nucleus are position isomers. Their properties are often so nearly alike as to present difficulties in identification or separation. *Ex parte Mowry* (POBA 1950) 91 USPQ 219. A novel, useful compound which is isomeric with a compound of the prior art is unpatentable unless it possesses some unobvious or unexpected beneficial property not possessed by the prior art compound. *In re Norris* (CCPA 1950) 179 F2d 970, 84 USPQ 458; *In re Finley* (CCPA 1949) 174 F2d 130 and 135, 81 USPQ 383 and 387.

A compound need not be an adjacent homolog or position isomer of a prior art compound in order to be susceptible to a rejection based on structural obviousness; the name used to designate the structural relationship between compounds is not controlling, it is the closeness of that relationship. *In re Payne et al.* (CCPA 1979) 606 F2d 303, 203 USPQ 245. When chemical compounds have "very close" structural similarities...without more, a *prima face* case of obviousness may be made. *In re Grabiak* (CAFC 1985) 769 F2d 729, 226 USPQ 870.

The prior art teaches the -OMe group in the para-position on the phenyl ring.

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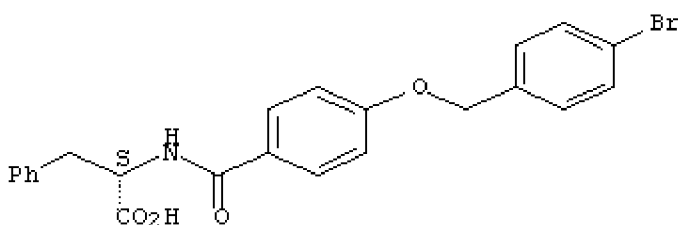
However, the current application claims this group as a substituent on the phenyl ring in any position. The rearrangement of the group into an adjacent position would be attempted by anyone skilled in the art who was attempting to make the compounds of Formula (I). The claims above are obvious because the rearrangement of the same group to an adjacent position would have yielded predictable results in the process to one of ordinary skill in the art at the time of the invention.

Claims 12, 14 and 46 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kundu, et. al., Combinatorial Chemistry and High Throughput Screening (2002), 5(7), 545-550, in view of *Graver Tank & Mfg. Co. v. The Linde Air Products Co.*, (USSC 1950) 339 US 695, 85 USPQ 328.

The prior art teaches the following compound 39 on page 546:

RN 524048-72-4 CAPLUS  
CN L-Phenylalanine, N-[4-[(4-bromophenyl)methoxy]benzoyl] - (CA INDEX NAME)

Absolute stereochemistry.



The court decision of *Graver Tank* teaches that the important factor in determining a test for equivalency in a prior art document is whether a person who is reasonably skilled in the art would recognize the equivalency in the compound or composition. In *Ex parte Wiseman* (POBA 1953) 98 USPQ 277, a difluorinated



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compound was held unpatentable over the prior art dichloro compound on the basis of analogical reasoning. A compound need not be an adjacent homolog or position isomer of a prior art compound in order to be susceptible to a rejection based on structural obviousness; the name used to designate the structural relationship between compounds is not controlling, it is the closeness of that relationship. In *re Payne et al.* (CCPA 1979) 606 F2d 303, 203 USPQ 245. When chemical compounds have “very close” structural similarities and similar utilities, without more, a *prima facie* case of obviousness may be made. In *re Grabiak* (CAFC 1985) 769 F2d 729, 226 USPQ 870.

Relating the information from *Graver Tank* to the Kundu et. al. publication, it would have been obvious for a person of ordinary skill in the art to synthesize the same compound and replace the chlorine atom of the prior art with a bromine or fluorine atom, which is claimed in the current application. The differences between fluorine, chlorine and bromine are well known in the chemical arts to have similar properties. For example, all three elements fall within the same family in the periodic table of the chemical elements. As atoms, fluorine, chlorine and bromine contain the same valence number, similar chemical properties and numerous chemical literature has suggested the attempted use of a fluorine or bromine over a chlorine group and vice versa. Due to the numerous chemical property similarities of fluorine, chlorine and bromine, this substitution would be attempted by anyone skilled in the art.

It would have been obvious to one skilled in the arts at the time of the invention to be motivated to synthesize the same compound and replace the chlorine atom for a fluorine or bromine atom. Kundu et. al. shows a chloro-substituted phenyl ring, and

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*Graver Tank* shows that fluorine, chlorine and bromine are chemical equivalents, and thus similar effects both chemically and biologically would be expected. Due to the numerous chemical property similarities of fluorine, chlorine and bromine, this substitution would be attempted by anyone skilled in the art who was attempting to make the compounds of Formula (I). The claims above are obvious because the substitution of one known element for another (fluorine, chlorine and bromine) would have yielded predictable results in the process to one of ordinary skill in the art at the time of the invention.

#### ***Allowable Subject Matter***

Claim 13 is objected to as being dependent upon an objected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Claims 13 is free of the prior art. The closest prior art is over Kundu, et. al., *Combinatorial Chemistry and High Throughput Screening* (2002), 5(7), 545-550. Kundu, et. al. teaches compounds of Formula (I) but does not teach the benzyloxyphenyl group in the 3-position.

#### ***Conclusion***

Claims 12, 14 and 46 are rejected.

Claim 46 is objected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey H. Murray whose telephone number is 571-272-9023. The examiner can normally be reached on Mon.-Thurs. 7:30-6pm EST.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisors, Mr. James O. Wilson can be reached at 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Jeffrey H Murray/  
Patent Examiner , Art Unit 1624